

REMARKS

Status of the Claims

Claims 1, 2, 5, and 7 – 10 are pending, with claim 1 being independent.

Claims 3 and 4 have been cancelled as being directed to non-elected subject matter pursuant to the restriction requirement without prejudice to or disclaimer of the subject matter contained therein. Applicants expressly reserve the right to file one or more divisional applications directed to the non-elected subject matter. Claim 6 has also been cancelled without prejudice to or disclaimer of the subject matter contained therein.

Without conceding the propriety of the rejections, claims 1, 2, and 5 have been amended to even more clearly recite and distinctly claim the present invention. New claims 7 – 10 have been added. Support for the amendments and new claims may be found in the original claims as well as throughout the specification, including, for example, at page 4. Therefore, no new matter has been added.

Applicants respectfully request the Examiner to reconsider and withdraw the outstanding rejections in view of the foregoing amendments and the following remarks.

Claim Rejections under 35 U.S.C. § 112

Claims 5 and 6 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly not being written in proper U.S. claim form. The Office Action asserts that the utility statement in claim 6 is not acceptable as collagenase/MMP-inhibiting activities are not real world activities. Without conceding the propriety of the rejections, claim 5 has been amended to even more clearly recite and distinctly claim the present invention; claim 6 has been cancelled without prejudice to or disclaimer of the subject matter contained therein; and new claims 7 – 10 have been added.

Applicants respectfully traverse the rejection regarding the utility of collagenase/MMP-inhibition.

Applicants respectfully submit that one of skill in the art would immediately appreciate that inhibiting collagenase/MMP activities in a mammal, as now recited in claim 7, is a specific, substantial, and credible utility. As such, Applicants respectfully submit that inhibiting collagenase/MMP activities in a mammal defines a real world context of use.

Applicants respectfully submit that one of skill in the art readily recognizes that the enzymatic activities of collagenase/matrix metalloproteinases (MMPs) are involved in various disease states including, rheumatic diseases, tumor metastasis and invasion, and UV-induced erythema. (specification, page 4). Applicants further respectfully submit that one of skill in the art readily recognizes that inhibition of collagenase/matrix metalloproteinases (MMPs) is involved in the healing of such diseases or in exerting a palliative effect on the pathological symptoms caused by these enzymes in these disease states. (specification page 3). In addition, in support of their assertion of the utility of inhibiting collagenase/MMP activities, Applicants provide the Examiner with literature references providing evidence that one of ordinary skill in the art readily recognized that inhibiting collagenase/MMP activities is a specific and substantial utility, which was well established. Accordingly, Applicants submit herewith the following literature references:

“Matrix Metalloproteinase Inhibitors: Current Developments and Future Perspectives,” *The Oncologist*, 2001; 6:415-427;

“The many faces of metalloproteases: cell growth, invasion, angiogenesis and metastasis,” *A TRENDS Guide to Cancer Biology*, 2001, S37-S43;

“Sequence-specific silencing of MT1-MMP expression suppresses tumor cell migration and invasion: importance of MT1-MMP as a therapeutic target for invasive tumors,” *Oncogene* (2003) 8716-8722; *Matrix Metalloproteinases* edited by William C. Parks and Robert P. Mecham, Academic Press;

“Low Collagenase-1 (MMP-1) and MT1-MMP Expression Levels Are Favourable Survival Markers in Advanced Colorectal Carcinoma,” *Oncology*, 2003, 65(4):337-46;

“Matrix metalloproteinase-7 and matrix metalloproteinase-9 are associated with unfavourable prognosis in superficial oesophageal cancer,” *Br J Cancer*, 2003 Dec 1, 89(11):2116-211; and

“Early combined treatment with carboplatin and the MMP inhibitor, prinomastat, prolongs survival and reduces systemic metastasis in an aggressive orthotopic lung cancer model,” *Lung Cancer*, 2003 Dec, 42(3):335-44.

By way of example, as set forth in the above literature references, inhibitors of MMP could block human fibrosarcoma cell invasion through reconstituted basement membranes and inhibit lung colonization by B16F10 mouse melanoma cells. Also by

way of example, as set forth in the above literature references, inhibitors of MMP could inhibit tumor growth either by encouraging the development of fibrotic tissue around the tumor, thereby preventing invasive growth, or by inhibiting angiogenesis. Further by way of example, as set forth in the above literature references, inhibitors of MMP have been shown to reduce the growth rate of tumors.

Therefore, Applicants respectfully submit that inhibition of collagenase/MMP activities in a mammal, as now recited in claim 7, is a specific, substantial, and credible utility well recognized by one of skill in the art. Accordingly, Applicants request withdrawal of the rejections under 35 U.S.C. § 112, second paragraph.

Claim Rejections under 35 U.S.C. § 103(a)

Claims 1 and 2 are rejected under 35 U.S.C. § 103 as allegedly being unpatentable over EP 0454060, DD 293816, and DD 293824. Applicants respectfully disagree with the rejection; therefore, this rejection is traversed.

EP 0454060 discloses compounds which have immunostimulatory and immunorestorative effects for use in disorders of the immune system and in viral infections, one of which is the compound to which the Examiner refers.

In contrast, the presently claimed compounds are compounds in which Alk* is C₂-C₁₂ branched or unbranched alkylene, with the exception of 3-methylpropylene [-CH₂-CH₂-CH(CH₃)-]. The presently claimed compounds exhibit pharmacologically significant collagenase/MMP-inhibiting activity.

Applicants respectfully submit that exhibiting collagenase/MMP-inhibiting activity is significantly different than exhibiting immunostimulatory and immunorestorative effects. Applicants respectfully submit that EP 0454060 does not disclose or suggest compounds exhibiting pharmacologically significant collagenase/MMP-inhibiting activity. Accordingly, Applicants respectfully submit that the presently claimed compounds have unexpected properties in that the presently claimed compounds exhibit collagenase/MMP-inhibiting activity. Applicants respectfully submit that obviousness based on structural similarity is rebutted since the claimed compounds exhibit unexpected properties. MPEP 2144.09. Therefore, Applicants respectfully submit that the presently claimed compounds are not obvious over EP 0454060.

DD 293816 and DD 293824 disclose only preparation methods for compounds. The compound in DD 293816 to which the Examiner refers is a starting compound for the synthesis of 3-(alkylthioalkyl)-2,4-dioxo-1,2,3,4-tetrahydrochinazolinene. The compound in DD 293824 to which the Examiner refers is a synthetic intermediate. It is respectfully submitted that the ultimate compounds prepared by the methods of preparation described in both DD 293816 and DD 293824 have immunomodulatory properties.

In contrast, the presently claimed compounds are compounds in which Alk* is C₂-C₁₂ branched or unbranched alkylene, with the exception of 3-methylpropylene [-CH₂-CH₂-CH(CH₃)-]. The presently claimed compounds exhibit pharmacologically significant collagenase/MMP-inhibiting activity.

Applicants respectfully submit that exhibiting collagenase/MMP-inhibiting activity is significantly different than exhibiting immunomodulatory properties. Applicants further respectfully submit that the compound in DD 293816 and DD 293824, to which the Examiner refers, is disclosed only as a starting material or a synthetic intermediate. Moreover, Applicants respectfully submit that DD 293816 and DD 293824 do not disclose or suggest compounds exhibiting pharmacologically significant collagenase/MMP-inhibiting activity. Accordingly, Applicants respectfully submit that the presently claimed compounds have unexpected properties in that the presently claimed compounds exhibit collagenase/MMP-inhibiting activity. Applicants respectfully submit that obviousness based on structural similarity is rebutted since the compounds DD 293816 and DD 293824 are only a synthetic starting material and a synthetic intermediate and the claimed compounds exhibit unexpected properties. MPEP 2144.09. Therefore, Applicants respectfully submit that the presently claimed compounds are not obvious over DD 293816 and DD 293824.

For at least the above explained reasons, it is respectfully submitted that EP 0454060, DD 293816, and DD 293824 do not disclose or suggest the presently claimed compounds.

Therefore, withdrawal of the rejections under 35 U.S.C. § 103 is respectfully requested.

Conclusion

Without conceding the propriety of the rejections, claims 1, 2, and 5 have been amended, as provided above, to even more clearly recite and distinctly claim Applicants' invention and to pursue an early allowance.

For the reasons noted above, the art of record does not disclose or suggest the inventive concept of the presently claimed invention as defined by the claims.

In view of the foregoing amendments and remarks, reconsideration of the claims and allowance of the subject application is earnestly solicited. The Examiner is invited to contact the undersigned at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted,

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